In the Claims

Please cancel Claims 47-49 and 71-72.

REMARKS

Claims 47-49 and 71-72 have been canceled. Claims 44-46, 50-51, 62-64, 67-70, 74 and 78-89 are pending.

Rejection of Claims under 35 U.S.C. 112, first paragraph

The Examiner maintained the rejection of Claims 44-51, 62-64, 67-72, 74 and 78-89, for reasons of record. Three issues remain under this rejection, each of which is addressed in turn.

Constructs

The Examiner stated that the constructs used in the Declaration under 37 C.F.R. 1.132 of Dr. Harriet L. Robinson, filed 2/28/96, referred to herein as the "Data Declaration," have different epitopes from those of the constructs in the specification, such that the results obtained using the constructs described in the Data Declaration cannot be correlated to those from the constructs described in the specification.

To address this matter, a Declaration under 37 C.F.R. 1.132 of Shan Lu, M.D. (referred to herein as the "Construct Declaration"), is being filed concurrently with this Amendment. As indicated in the Construct Declaration, the constructs described in the Data Declaration are the same as those described in the specification: thus, one of ordinary skill in the art would expect them to have the same epitopes as one another, and to behave in the same manner as each other under the same experimental conditions. Thus, the results described in the Data Declaration do, in fact, correlate with results from the constructs described in the specification.

Immunization

The Examiner stated that it was not clear that the animals described in the Data Declaration had any level of protection from disease manifestation.

As described in the Specification at page 7, lines 5-11, "immunizing" refers to production of an immune response which protects, partially or totally, from the manifestations of infection (i.e., disease) caused by the infectious agent, in that the individual immunized will not be

infected, or will be infected to a lesser extent, than would occur without immunization. Thus, "protection" refers not only to a change in susceptibility to the disease, but also, can refer to generation of an immune response that lessens or eliminates manifestations of infection.

The experiments described in the Data Declaration relate to assessment of the ability of a nucleic acid vaccine to protect against disease in a highly virulent, uncloned SIVmac251 rhesus macaque model. The virus used generally causes $\geq$ 50% incidence of AIDS during the first year of infection (see, e.g., description of the virulence of the particular virus in Lu, S. *et al.*, "Simian Immunodeficiency Virus DNA Vaccine Trial in Macaques," *J. Virol. 70(6)*:3978-3991 (1996), a copy of which is attached as Exhibit A; this reference contains the information previously submitted in the Data Declaration). In the case of highly virulent models, partial protection, rather than complete protection, against disease is usually expected.

As described in the Data Declaration, a more rapid reduction of viral loads to chronic levels was achieved in the immunized animals, in comparison to the rate of reduction in control animals. The ability of the vaccinations to effect such a rapid reduction of viral loads was particularly noteworthy in view of the virulence of the challenge virus. If a less virulent challenge virus were used, one could reasonably expect that even greater protection (e.g., further reduction of viral loads or other protective immune responses) could be achieved.

Furthermore, rapid reduction of viral load is indicative of a response which protects, at least partially, against manifestations of disease, by attenuating the acute phase of infection. Attenuation of the acute phase of infection also reduces transmission of infection, by reducing the window of time in which an individual has a high virus load, and thus is particularly useful in a virulent model where complete protection may not be expected (see, e.g., Lu *et al.*, *supra*, p. 3989, "Protection of a population as opposed to protection of the vaccinated individual").

Model

The Examiner stated that the macaque model is not recognized as predictive for HIV vaccination, and provides three references from the mid-to-late 1990's (1994, 1996, and 1998), all of which were published after the filing date of the current application. These references were cited to rebut the four references from the early 1990's previously cited by Applicants regarding the use of the macaque model as an important animal model for infection of humans with HIV (i.e., Gardner, M.B., *Antiviral. Res. 15*:267-286 (1991); Gardner, M.B., *Dev. Biol. Stand. 72*:259-266 (1990); Johnson, P.R. and Hirsch, V.M., *Int. Rev. Immunol. 8*:55-63 (1992); and

McClure, H.M. *et al., Ann. NY Acad. Sci. 616*:287-298 (1990)). The references previously cited by Applicants were selected, in part, because they demonstrate the state of the art at the time the application was filed. One of ordinary skill in the art, given the specification and the state of the art at the time the application was filed, as demonstrated by the references previously cited by Applicants, would find the macaque model described in the specification and used in the Data Declaration to be an appropriate model that would be predictive for HIV vaccination.

Rejection of Claims under 35 U.S.C. 112, second paragraph

The Examiner maintained the rejection of Claims 47-49 and 71-72, stating that the claims remained indefinite. Solely to expedite prosecution, these claims have been canceled.

CONCLUSION

In view of the amendments and discussion presented above and the accompanying Declaration of Dr. Lu, the claims are in condition for allowance. Applicant's Attorney respectfully requests reconsideration and withdrawal of the remaining rejections.

If the Examiner believes that a telephone conversation would expedite prosecution of the application, the Examiner is invited to call Elizabeth W. Mata at (915) 845-3558. If Elizabeth W. Mata cannot be reached, the Examiner is invited to call David E. Brook at (781) 861-6240.

Respectfully submitted,

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